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# Flow cytometry screening strategy for the enrichment of high-producing Chinese Hamster ovary cells for monoclonal antibody manufacturing

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Establishment of Chinese hamster ovary (CHO) cell lines for the production of monoclonal antibodies (mAbs) is generally conducted through transfection and pooling procedures with a laborious and time-consuming screening. It could be one of the most rate-limiting steps in the process development of mAb manufacturing. Therefore, an improvement to screening efficiency will give a positive impact to shortening the period of process development. We here propose an enrichment strategy for screening for high-producing cells using flow cytometry (FCM).

A stable pool prepared by mAb-expression vector transfection was stained with a fluorescent-labeled antibody that binds to an mAb presented on the cell surface and was applied to FCM analysis and cells were separated and grouped based on their fluoresence. The volumetric productivity in a fed-batch culture of grouped cells, which showed the brightest of fluorescein isothiocyanate (FITC)-positive cells, was only 1.2 to 1.3 times higher than that of ungrouped cells, despite our expectation. Therefore, we tried to set the cell size and intracellular density gates based on forward scatter (FSC) and side scatter (SSC), and selected the brightest 5% of FITC-positive cells from each group by FCM. The volumetric productivity of cells gated by FSC and SSC was 3.4- to 4.7-fold higher than ungrouped cells. Surprisingly, the selection with the highest volumetric productivity indicated the smallest value of FSC and SSC, and the middle value of fluorescence intensity among all selected cells. Our results showed that our new screening strategy by FCM to group cells with the smallest values of FSC and SSC based on FSC and SSC gates could achieve an efficient enrichment of high-producing cells.